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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/499,006	02/04/2000	Dr. Paddy Jim Baggot	249/127	9604

34313 7590 04/27/2004

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/499,006	BAGGOT, DR. PADDY JIM	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 15-24* is/are pending in the application.

4a) Of the above claim(s) *1, 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-16 and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 8, 2004 has been entered.

2. Claims 15, 18-19, and 21-24 have been amended. Claims 15-16 and 18-24 are now under consideration. Claims 1 and 17 remain withdrawn from consideration. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims.

Election/Restriction

3. Claims 1 and 17 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

Claim Objections

4. Claims 21-23 are objected to because of the following informalities: claim 21 recites the limitation "in amniotic fluid a fetus with Down Syndrome" rather than, e.g., "in amniotic fluid of a fetus with Down Syndrome;" claim 21 also includes a period (rather than a comma) at the end of the "obtaining a control profile" step of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 15-16 and 18-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to methods of "identifying Down Syndrome in a fetus" comprising obtaining an amniotic fluid specimen, identifying "a quantity for each metabolite that is present in the amniotic fluid specimen," and comparing a profile of metabolites in the specimen with a control profile, wherein Down Syndrome is identified when "a pattern of the quantity of each metabolite" differs from a pattern in a control profile representing normal levels of metabolites in amniotic fluid (claims 15-16, 18-20, and 24) or when a pattern of abnormal quantities of metabolites identified in the specimen are further found to correspond to a pattern present in amniotic fluid of a fetus with Down Syndrome. It is unpredictable as to whether one of skill in the art could use the claimed invention. The specification discloses that the mean and median levels of several metabolites in a population of "Down Syndrome patients" differ from the mean and median levels found in a population of "normal patients" (see data presented at pp. 7-16). However, the specification does not disclose the identity of the body fluid employed to produce the data provided in the specification. For example, it is unknown

based on the guidance provided in the specification as to whether the levels disclosed in the specification were detected in, e.g., the blood of patients suffering from Down Syndrome or in amniotic fluid obtained from mothers carrying fetuses with Down Syndrome (as recited in the instant claims). Thus, the specification does not provide evidence that one may diagnose or identify Down Syndrome in a fetus by comparing levels of metabolites in amniotic fluid. Further, it is unpredictable as to how the relative levels of metabolites detected in, e.g., the blood of a patient suffering from Down Syndrome would relate to the relative levels of metabolites found in the amniotic fluid of a mother carrying a child with Down Syndrome. Absent guidance from the specification, one of skill in the art may rely on the teachings of the prior art for enablement of a claimed invention. However, in the instant case, the prior art is silent with respect to methods in which differences in the quantities of a plurality of metabolites in amniotic fluid are employed in the diagnosis of Down Syndrome. Thus, neither the specification nor the art provide evidence that one may diagnose Down Syndrome in a fetus by comparing levels of a group of amniotic fluid metabolites with levels from a normal control population. Further, neither the specification nor the art establish a correlation between levels of metabolites in amniotic fluid surrounding a fetus with Down Syndrome and, e.g., levels in blood of an adult Down Syndrome patient. As it is unknown as to whether differences in amniotic fluid metabolite levels actually exist in Down Syndrome patients as compared to normal patients, it is further unpredictable as to whether any quantity of experimentation would be sufficient to allow one of skill in the art to practice the invention as claimed, and the level of experimentation required to use the claimed

invention is therefore undue. Further, it is noted that the teachings of the specification indicate that only particular metabolites exhibit significant differences in Down Syndrome patients as compared to normal patients. Were the specification to have identified the body fluid employed in obtaining the data at pages 7-16, the teachings of the specification would enable one of skill in the art to identify Down Syndrome by detecting differences in a levels of a subset/plurality of metabolites that were shown by Applicant to exhibit significant differences in a Down Syndrome population as compared to a normal population. However, as it is unpredictable as to whether any other metabolites exhibit such significant differences in levels, it would require undue experimentation to practice the invention as it is broadly claimed.

With regard to the prior rejection of the instant claims for lack of enablement, the response traverses the rejection on the following grounds. The response argues that "the Office Action is not correct to suggest that the present invention generates only patient profiles," but that the "specification is, in fact, an exemplification of the diagnosis of chromosomal abnormalities in a fetus." The response states that "The reference to the use of chromosomal abnormalities in 'patients,' suffering from Down Syndrome is a result of the fact that the data used to generate the control profile is obtained from the amniotic fluids of fetuses who have been born and conclusively diagnosed later as 'patients' with Down Syndrome." Applicant argues that "this terminology is used in ordinary medical practice and in the present specification because this data, while based on amniotic fluid samples taken from a number of fetuses, is confirmed and assigned to a profile group by a postpartum diagnosis, and this diagnosis is part of

developing the appropriate control profile." The response notes the need for developing an "appropriate control profile," and states that "Once established, the control profile is used to compare the amniotic fluid specimen obtained from the womb and the practice of the method of the invention is performed." The response indicates that the claimed method is "a diagnosis of chromosomal abnormalities in the fetus to diagnose Down Syndrome, and a previously developed profile from control patients is used," and further that the claims have been amended "to clarify the nature of the diagnosis being performed." Regarding the term "patient" as used in the specification, the response continues that "this use is ordinary practice in the field when referring to data obtained from amniotic fluid, even though a subsequent diagnosis may be made post-partum." The response urges that the specification "provides data obtained from the amniotic fluid of a fetus and ultimately used in comparison with a profile of metabolite concentrations that are similarly obtained, but whose diagnosis, i.e., assignment to either a control or Down Syndrome population is achieved by post-partum testing." The response further states that "Applicant has extensive data that could be provided by declaratory evidence that the amniotic fluid obtained from a fetus may be used in comparison with a profile of control group, i.e., healthy babies, to diagnose Down Syndrome" and that "Applicant is readily capable of providing declaratory data that is ordinary practice of those skilled in the art to use the term 'patient' to describe data obtained in this manner and used in this manner as the basis for analysis of a future specimen." The response concludes that "the example in the specification is an exemplification of the claimed method and does not merely refer to the generation of

patient profiles, but to the diagnosis of Down Syndrome from the amniotic fluid of the fetus."

Applicant's arguments have been thoroughly considered but are not persuasive. First, with regard to Applicant's argument that the specification exemplifies the diagnosis of chromosomal abnormalities in a fetus using amniotic fluid, it is noted that while Applicant's arguments clearly state that amniotic fluid samples were employed in the methods exemplified in the specification, the specification itself does not indicate this. One of skill in the art must rely on the guidance provided in the specification (not in Applicant's arguments). As discussed above, the specification discloses that the mean and median levels of several metabolites in a population of "Down Syndrome patients" differ from the mean and median levels found in a population of "normal patients" (see data presented at pp. 7-16); however, the specification does not disclose the identity of the body fluid employed to produce the data provided in the specification, and further does not indicate that the term "patient" refers to a fetus. Given the vagueness of the specification, one of skill is left to draw his or her own conclusions regarding what would constitute a "Down Syndrome patient" and a "normal patient," and with regard to the type of body fluid employed in producing Applicant's data. The response argues that the term "patient" was employed because fetuses were "conclusively diagnosed later as 'patients' with Down Syndrome;" however, the specification itself does not state or otherwise indicate this. Further, this argument suggests that the term "patient" in fact refers to individuals who have been born and are known to have Down Syndrome, rather than to a fetus who has yet to be conclusively diagnosed with a condition. Thus,

this argument reinforces the examiner's point that the term "patient" is typically employed when referring to an individual who has a condition, as opposed to a fetus who is not yet considered to be a "Down Syndrome patient." It is again noted that the specification does not indicate that the term "patient" is used in the specification to refer to a fetus or "fetal patient." Regarding Applicant's argument that the term patient "is used in ordinary medical practice" to refer to a fetus, it is noted that Applicant has yet to provide any evidence or references to support this assertion. While the response states (as was stated in an earlier response) that declaratory evidence regarding this use of the term "patient" can be provided, no such evidence has been submitted. Similarly, Applicant has yet to provide the referenced declaratory evidence regarding the use of amniotic fluid in practicing the invention. Thus, Applicant's arguments are not persuasive.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS TO THE CLAIMS.

8. Claims 15-16 and 18-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15-16, 18-20 and 24 are indefinite over the recitation of the phrase "identifying the presence of Down Syndrome in the fetus when a pattern of the quantity of each metabolite in the amniotic fluid specimen differs from a pattern in the quantity of

each metabolite in the control profile." It is unclear as to what might be considered a "pattern of the quantity of each metabolite," and as to how a "pattern of the quantity" of a metabolite would differ from the quantity of the metabolite (i.e., does the claim require a comparison of quantities, or of some particular feature or "pattern" of each quantity?). Clarification is required.

Claim 16 is indefinite over the recitation of the limitation "the subset of metabolites" because there is insufficient antecedent basis for this recitation in the claims.

Claims 21-23 are indefinite over the recitation of the phrase "identifying the presence of Down Syndrome in the fetus when a pattern of the quantity of each metabolite in the profile of the amniotic fluid specimen corresponds to a pattern of the quantity of each metabolite in amniotic fluid a fetus with Down Syndrome." It is unclear as to what might be considered a "pattern of the quantity of each metabolite," and as to how a "pattern of the quantity" of a metabolite would differ from the quantity of the metabolite (i.e., does the claim require a comparison of quantities, or of some particular feature or "pattern" of each quantity?). Clarification is required.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Diana B. Johannsen
Patent Examiner
April 26, 2004